

**IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY**

BRISTOL-MYERS SQUIBB COMPANY,

Plaintiff,

v.

APOTEX, INC., and
APOTEX CORP.

Defendants.

Civil Action No. 3:10-cv-05810 (MLC)(LHG)

Electronically Filed

**Deadline for Responsive Claim
Construction: June 4, 2012**

PLAINTIFF'S OPENING CLAIM CONSTRUCTION BRIEF

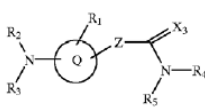
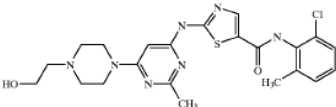
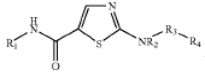
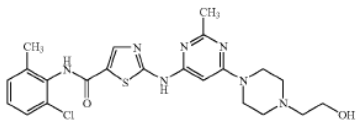
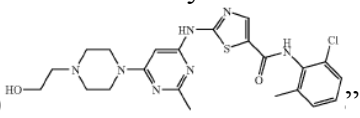
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Plaintiff Bristol-Myers Squibb Company (“BMS”) respectfully provides its Opening Claim Construction Brief in support of its proposed construction of certain terms¹ of U.S. Patent Nos. 6,596,746 (“the ‘746 patent”), 7,125,875 (“the ‘875 patent”), 7,153,856 (“the ‘856 patent”) and 7,491,725 (“the ‘725 patent”).

I. INTRODUCTION

BMS markets Sprycel[®] (dasatinib), a drug that is indicated for treating, *inter alia*, chronic myeloid leukemia (“CML”) and has enjoyed extensive sales in the United States totaling approximately \$294 million in 2011. Sprycel[®] and its methods of use are covered by the ‘746 patent,² the ‘875 patent,³ the ‘856 patent,⁴ and the ‘725 patent.⁵ The ‘746 patent claims, *inter alia*, the compound dasatinib, which is the active pharmaceutical ingredient in Sprycel[®]. The ‘875 patent claims methods of using dasatinib to treat cancer, including treatment of CML. The ‘856 patent claims methods of using dasatinib to treat cancer via oral administration. The ‘725 patent claims, *inter alia*, a crystalline monohydrate form of dasatinib.

The ‘856 patent issued from a continuation application of the ‘746 patent. The ‘875 patent issued from a continuation-in-part application of the ‘746 patent. Thus, the ‘746, ‘875, and ‘856 patents have identical disclosures other than the additional matter in the ‘875 patent. The ‘725 patent has no relationship with the other three patents and has a different disclosure.

BMS is asserting infringement of claims 6, 7, 18, 27-30, 32, 33, 42-44, 46 and 47 of the ‘746 patent, claim 1 of the ‘856 patent, claims 1-3, 5, 7, 9-12, and 27 of the ‘875 patent, and

¹ The list of the terms on which the parties agree to their construction are identified in Ex. A to the Certification of Christine I. Gannon in Support of Plaintiff’s Opening for Claim Construction Brief (hereinafter “Gannon Cert.”) The list of disputed terms, together with each party’s proposed constructions are attached as Gannon Cert. Ex. B.

² The ‘746 patent is attached to Dr. Jorgensen’s Declaration as Ex. A (“Jorgensen Ex. A”).

³ The ‘875 patent is attached to Dr. Jorgensen’s Declaration as Ex. C (“Jorgensen Ex. C”).

⁴ The ‘856 patent is attached to Dr. Jorgensen’s Declaration as Ex. B (“Jorgensen Ex. B”).

⁵ The ‘725 patent is attached to the Dr. Atwood’s Declaration as Ex. A (“Atwood Ex. A”).

claims 1-16 of the '725 patent against defendants Apotex, Inc. and Apotex Corp. (collectively "Apotex"), which have submitted Abbreviated New Drug Application ("ANDA") No. 202-103 and No. 203-180 seeking approval from the U.S. Food and Drug Administration ("FDA") to market generic versions of Sprycel[®].

The meaning of twenty terms of these asserted claims are currently in dispute. BMS's proposed constructions of these terms are largely based on the intrinsic record and the ordinary meaning of these terms as understood by one of ordinary skill in the art, and are consistent with the tenets of claim construction set forth in Federal Circuit's *en banc* decision *Phillips v. AWH Corp.* BMS submits that many of the terms being construed are readily understandable to one of ordinary skill and do not require construction by the Court. Where certain terms do require construction, the meanings of those terms are generally clearly set forth in the specification or other intrinsic evidence. It is this plain meaning and intrinsic evidence that BMS's proposed constructions follow.

Apotex, on the other hand, having no viable non-infringement or invalidity positions, identified dozens of claim terms that it contends require construction or are indefinite. Apotex's proposed constructions find little or no support in the intrinsic evidence. Apotex's aim is plainly to throw enough "mud" in the hope that some will stick. BMS respectfully submits the Court should not be persuaded by Apotex's misguided approach, and should adopt BMS's constructions — which closely align with the ordinary meaning of the claim terms and the patents' teachings.

II. LAW OF CLAIM CONSTRUCTION

"[I]nterpretation and construction of patent claims, which define the scope of the patentee's rights under the patent, is a matter of law exclusively for the court." *Markman v. Westview Instr., Inc.*, 52 F.3d 967, 970-971 (Fed. Cir. 1995), *aff'd*, 517 U.S. 370 (1996). When

construing the claims of a patent, a court first considers the literal language of the claim, the patent specification and the prosecution history. *Id.* at 979. In *Phillips v. AWH Corp.*, the *en banc* Federal Circuit reaffirmed the “bedrock principle” of patent law that “the claims of a patent define the invention to which the patentee is entitled the right to exclude.” 415 F.3d 1303, 1312 (2005) (citation omitted). “Because the patentee is required to ‘define precisely what his invention is,’ the court explained, it is ‘unjust to the public, as well as an evasion of the law, to construe it in a manner different from the plain import of its terms.’” *Id.* (quoting *White v. Dunbar*, 119 U.S. 47, 52 (1886)).

Accordingly, claim construction starts with the words of the claims themselves, which “are generally given their ordinary and customary meaning” as would have been understood by a person of ordinary skill in the art at the time of the invention and which can “provide substantial guidance as to the meaning of particular claim terms.” *Phillips*, 415 F.3d at 1312-1314 (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)). Importantly, “the person of ordinary skill in the art is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification.” *Id.* at 1313.

The ordinary and customary meaning understood by such a person provides the “objective baseline” for the claim’s construction. *Id.* Thus, the claim language itself is first and foremost in importance when construing the meaning and scope of the patent. *See Johnson Worldwide Assocs., Inc. v. Zebco Corp.*, 175 F.3d 985, 989 (Fed. Cir.1999). The general rule is “that terms in the claim are to be given their ordinary and accustomed meaning” and “general descriptive terms will ordinarily be given their full meaning; modifiers will not be added to broad terms standing alone.” *Johnson Worldwide*, 175 F.3d at 989. In short, a court must

presume that the terms in the claim mean what they say, and, unless otherwise compelled, give full effect to the ordinary and accustomed meaning of claim terms. *Id.* Thus, if the claim is unambiguous and clear on its face, the court need not consider the other intrinsic evidence. *See Smiths Indus. Med. Sys., Inc. v. VitalSigns, Inc.*, 183 F.3d 1347, 1357 (Fed. Cir. 1999) (citing *Renishaw PLC v. Marposs Societa per Azioni*, 158 F.3d 1243, 1248-49 (Fed. Cir. 1998)).

When the meaning is unclear or more than one meaning could be assigned, claim terms should be construed “in view of the specification” which “is always highly relevant to the claim construction analysis” – indeed, it is usually “dispositive.” *Phillips*, 415 F.3d at 1315 (citations omitted). The Federal Circuit informs that the specification “is the primary basis for construing the claim” and is in most cases “the best source for understanding a technical term.” *Id.*; *see also CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366 (Fed. Cir. 2002). Courts may also consider a patent’s prosecution history when construing claims. *Phillips*, 415 F.3d at 1317.

After examining the intrinsic evidence of the patent, if the meaning of the claim language is still ambiguous, the court may consider extrinsic evidence, “if necessary to aid the court’s understanding of the patent.” *See Wright Med’l Tech., Inc. v. Osteonics Corp.*, 122 F.3d 1440, 1443 (Fed. Cir. 1997).

In addition, “determination of claim indefiniteness is a legal conclusion that is drawn from the court’s performance of its duty as the construer of patent claims.” *Exxon Research and Eng’g Co. v. United States*, 265 F.3d 1371, 1376 (Fed. Cir. 2001). A claim is not indefinite merely because its scope is not ascertainable from the face of the claims. Rather, “a claim is indefinite under § 112 ¶ 2 if it is ‘insolubly ambiguous, and no narrowing construction can properly be adopted.’” *Id.* at 1375.

III. CONSTRUCTION OF TERMS IN THE ‘746, ‘875, AND ‘856 PATENTS

A. “A compound or salt thereof selected from the group consisting of”

The phrase “[a] compound or salt thereof selected from the group consisting of” appears in claim 6 of the ‘746 patent, which is directed to a compound or salt selected from a list of compounds that includes dasatinib. The parties’ proposed constructions are set forth below:

BRISTOL-MYERS CONSTRUCTION	APOTEX CONSTRUCTION
Plain meaning as understood by a person of ordinary skill in the art. “Salt” denotes acidic and/or basic salts formed with inorganic and/or organic acid and bases. In addition, “selected from the group consisting of” is a well accepted form of alternative expression commonly referred to as a Markush group. Thus, any pharmaceutical composition containing a compound listed in this claim would fall within the scope of the claim.	One compound or salt thereof selected from the following group of compounds; where the term “salt” denotes acidic and/or basic salts formed with inorganic and/or organic acids and bases; including zwitterions (internal or inner salts) and quaternary ammonium salts, and including both pharmaceutically- acceptable and other salts; prodrugs and solvates of the compound or salt thereof, and stereoisomers of the compound or salt thereof. The claim term is also understood to include all polymorphs of the compound or salt thereof. By virtue of its use of the language “selected from the group consisting of,” this term excludes those compositions containing one or more compounds not claimed in claim 6, including, but not limited to, for example, impurities.

BMS asserts this claim term should be given its ordinary, plain meaning as understood by a person of ordinary skill in the art, namely a compound or its salt selected from the claimed list. As stated above, a court must presume that the terms in the claim mean what they say, and, unless otherwise compelled, give full effect to the ordinary and accustomed meaning of claim terms. *Johnson Worldwide*, 175 F.3d at 989.

Claim 6 recites “[a] compound or salt thereof selected from the group consisting of [list of compounds].” The phrase “selected from the group consisting of” is a well accepted form of alternative expression commonly referred to as a Markush group, which limits the claimed “compound or salt thereof” to the compounds enumerated in the list of compounds and/or salts recited in claim 6. *See* Manual of Patent Examining Procedure (“M.P.E.P.”) § 2173.05(h) (8th

ed. 2001). In addition, the '746 patent defines "salt" as denoting "acidic and/or basic salts formed with inorganic and/or organic acid and bases." (Jorgensen Ex. A, col. 6, ll. 21-23).

Apotex's proposed construction is no construction at all, but rather a veiled attempt to present arguments about infringement and validity. Apotex argues that the term "selected from the group consisting of," "excludes those *compositions* containing one or more compounds not claimed in claim 6, including, but not limited to, for example, impurities." (Emphasis added.) Apotex's construction makes no sense. Claim 6 is drawn to a *compound*, not a composition. "[C]ompound claims include within their scope the recited compounds as chemical species in any surroundings." *Schering Corp. v. Geneva Pharms.*, 339 F.3d 1373, 1381 (Fed. Cir. 2003). The "selected from the group consisting of" language merely restricts the selection of the "compound or salt thereof" to those enumerated in claim 6, but does not dictate the manner in which the "compound or salt thereof" is combined with other substances outside the Markush group, for instance in a pharmaceutical composition. *See Teva Pharm. USA Inc. v. Amgen, Inc.*, 2010 U.S. Dist. LEXIS 95288, at *20-21 (E.D. Pa. Sep. 10, 2010) (rejecting construction that use of a Markush group means that "there can be only one member of the Markush group present in a product, and, if there are more, then the product is outside the scope of the patent").

In fact, the '746 patent clearly discloses that a composition can contain ingredients other than the listed compounds:

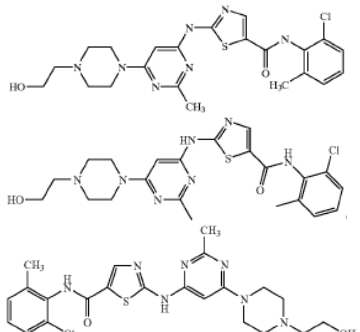
The compositions of the present invention may contain other therapeutic agents as described below, and may be formulated, for example, by employing conventional solid or liquid vehicles or diluents, as well as pharmaceutical additives of a type appropriate to the mode of desired administration (for example, excipients, binders, preservatives, stabilizers, flavors, etc.) according to techniques such as those well known in the art of pharmaceutical formulation.

(Jorgensen Ex. A, col. 25, ll. 27-35.) Accordingly, “a compound or salt thereof selected from the group consisting of” should be given its plain meaning.

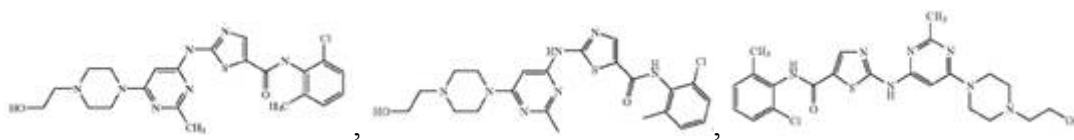
Apotex’s assertion that the Markush group of claim 6 excludes impurities is also baseless. A person of ordinary skill in the art would understand it is impossible to have a compound that is 100% free of impurities. *See* Declaration of William L. Jorgensen in Support of Plaintiff’s Opening Claim Construction Brief (“Jorgensen”) ¶¶ 8-9; *Ortho-McNeil Pharm., Inc. v. Mylan Labs., Inc.*, 348 F. Supp. 2d 713, 730 (N.D. W.Va. 2004), *aff’d*, 161 Fed. Appx. 944 (Fed. Cir. 2005) (“[A]lthough one of ordinary skill in the art would have understood the claim to the compound [] to be substantially pure [compound], the realities of science would have led such a skilled artisan to conclude that the purity was not 100 percent.”). Further, courts have consistently held that in the context of chemical patents “consisting of” does not exclude impurities. *Conoco, Inc. v. Energy & Environ. Int’l*, 460 F.3d 1349, 1360 (2006) (construing “‘consisting of’ to ‘close[] the claim to the inclusion of materials other than those recited except for impurities ordinarily associated therewith’”) (*quoting Ex parte Davis*, 80 U.S.P.Q. 448, 450 (Pat. Office Bd. App. 1948)); *Novo Nordisk v. Eli Lilly Co.*, 1999 WL 1094213, at *13 (D. Del. Nov. 18, 1999) (“Therefore, in the context of chemical patents, ‘consisting of’ indicates closed claim language and closes the claim to the inclusion of unrecited elements, except for impurities ordinarily associated therewith.”). Apotex’s construction should therefore be rejected.

B. Chemical names identified in claim 6 including but not limited to “N-(2-Chloro-6-methylphenyl)-2-[[6-[4-(2-hydroxyethyl)-1-piperazinyl]-2-methyl-4-pyrimidinyl]amino-5-thiazolecarboxamide.”

The chemical name “N-(2-Chloro-6-methylphenyl)-2-[[6-[4-(2-hydroxyethyl)-1-piperazinyl]-2-methyl-4-pyrimidinyl]amino-5-thiazolecarboxamide” is one of the names listed in the Markush group in claim 6 of the ‘746 patent. The parties’ proposed constructions are below:

BRISTOL-MYERS CONSTRUCTION	APOTEX CONSTRUCTION
<p>‘N-(2-Chloro-6-methylphenyl)-2-[[6-[4-(2-hydroxyethyl)-1-piperazinyl]-2-methyl-4-pyrimidinyl]amino]-5-thiazolecarboxamide represents the compound having the following equivalent chemical structures:</p> 	<p>The chemical descriptors given in claim 6 require the plain and ordinary meaning of such terms, to be interpreted according to IUPAC nomenclature guidelines.</p>

BMS’s proposed construction is consistent with its plain meaning as understood by one of ordinary skill in the art. One of ordinary skill in the art would understand the chemical name “‘N-(2-Chloro-6-methylphenyl)-2-[[6-[4-(2-hydroxyethyl)-1-piperazinyl]-2-methyl-4-pyrimidinyl]amino]-5-thiazolecarboxamide” identifies a compound having the following equivalent chemical structures, among others:



See Jorgensen ¶¶ 10.

Apotex similarly asserts this term should be given its plain meaning; however, its proposed claim construction is flawed in that it erroneously assumes the IUPAC nomenclature guidelines is the only way in which a compound can be named. Rather, there are several naming conventions used in the art. See Jorgensen ¶¶ 14, 15, 20, 22. For example, a given compound name can result in chemical structures that are illustrated in different ways, *i.e.*, with or without the hydrogen or carbon atoms explicitly shown, and a given chemical structure can have several proper names. See *id.* Apotex’s proposed construction should therefore be rejected.

C. “administering to” and “administering orally to”

The phrases “administering to” and “administering orally to”⁶ appear in claims 7, 44 and 47 of the ‘746 patent, claim 1 of the ‘856 patent, and claims 1, 2, 3, 11, and 27 of the ‘875 patent.

The parties proposed constructions are set forth below:

BRISTOL-MYERS CONSTRUCTION	APOTEX CONSTRUCTION
To mete out or dispense or to give remedially [the compound in oral form, including but not limited to tablets, capsules, granules or powders.]	The claim term requires two actors: one, the subject in need of treatment; two, another person, likely a physician, nurse practitioner or other clinician, responsible for giving the therapeutic agent in question. [Administration may be accomplished via any oral route (including but not limited to, in the form of tablets, capsules, granules or powders).] Further, a therapeutic agent may be administered either alone or in combination with other therapeutic agents, where the claimed compounds are administered either prior to, simultaneously with, or following administration of the other therapeutic agents. Administration may occur in a single dose or in individual divided doses.

Because the specification of the ‘746 patent does not specifically define the term “administering to,” the Court may consider extrinsic evidence, “if necessary to aid the court's understanding of the patent.” *See Wright*, 122 F.3d at 1443. Dictionaries are “among the many tools that can assist the court in determining the meaning of particular terminology to those of skill in the art of the invention.” *Phillips*, 415 F.3d at 1318; *see also ERBE Elektromedizin GmbH v. Int’l Trade Comm’n*, 566 F.3d 1028, 1036 (Fed. Cir. 2009). Consistent with BMS’s proposed construction, “administer” is defined in the dictionary as “to mete out” or “to give remedially.” *Merriam-Webster's Collegiate*[®] *Dictionary* 15 (Tenth Edition, 1993) (attached herein as Gannon Ex. C) (BMS01380830-32). *See Acorda Therapeutics Inc. v. Apotex Inc.*, 2011 WL 4074116, at *3, 26 (D.N.J. 2011) (finding that “administering” means “giving, prescribing, dispensing, dosing, self-dosing or taking”).

⁶ The additional proposed construction language corresponding to “orally” is contained in brackets in both parties proposed constructions.

In addition, the ‘746 patent specifically discloses that the claimed compounds may be administered “by any suitable means” including orally, sublingually, buccally, parenterally, nasally, topically or rectally. (Jorgensen Ex. A, col.25, ll. 36-54.) Therefore, the term “administering” should be construed without reference to particular routes of administration unless specified in the claim.⁷ *See Novo Nordisk* 1999 WL 1094213, at *16-17 (“administering” not limited to a particular route or routes). Accordingly, “administering to” should be construed as “to mete out or dispense or to give remedially.”

Apotex’s construction seeks to improperly impose extraneous limitations to the claims arguing that “administering to” should be construed to require “two actors.” *See Purdue Pharma L.P. v. Endo Pharms., Inc.*, 438 F.3d 1123, 1136-37 (Fed. Cir. 2006) (holding that it is impermissible to import an extraneous limitation into the claims); *Aventis Pharma S.A. v. Hospira, Inc.*, 2012 U.S. App. LEXIS 7095, *7 (Fed. Cir. April 9, 2012) (“We previously have refused to impose such limitations when not required by the language of the claims or the specification, and decline to do so here.”) (citations omitted). Apotex fails to identify any support in the intrinsic record -- the claim language, the specification, or the prosecution history -- to import the “two actors” limitation into the claim. *See Decisioning.com, Inc. v. Federated Dep’t Stores, Inc.*, 527 F.3d 1300, 1313 (Fed. Cir. 2008) (holding that the district court erred by adding limitations that were not required by the claim language or specification). Further, the *Acorda* court specifically stated that given its construction of “administering” -- giving, prescribing, dispensing, dosing, self-dosing or taking -- which is nearly identical to BMS’s proposed construction -- “a physician, pharmacist, or patient could alone infringe the patent.” 2011 WL 4074116, at *27. Apotex’s proposed construction should be rejected.

⁷ Claims 11 and 27 of the ‘875 patent and claim 1 of the ‘856 patent specify “oral” administration.

D. “a subject in need thereof”

The phrase “a subject in need thereof” appears in claims 7, 44 and 47 of the ‘746 patent, claim 1 of the ‘856 patent, and claims 1, 2, 3, 11, and 27 of the ‘875 patent. The parties’ proposed constructions are set forth below:

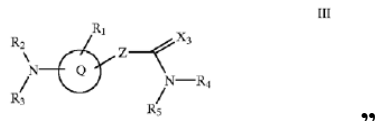
BRISTOL-MYERS CONSTRUCTION	APOTEX CONSTRUCTION
An animal, including a human, in need thereof	Any living organism having a protein-kinase associated disorder known to be susceptible to treatment with compounds of formula III, as construed above, as diagnosed by a second party, likely a physician or other clinician.

Unlike Apotex’s proposed construction, BMS’s proposed construction properly uses the specification to inform the meaning of “a subject in need thereof” by considering what the inventors described as their invention. The patent states that “[p]referred subjects for treatment include *animals*, most preferably mammalian species such as humans, and domestic animals such as dogs, cats and the like” (Jorgensen Ex. A, col. 26, ll. 53-57.) (emphasis added). Because the specification “is the primary basis for construing the claim” and is in most cases “the best source for understanding a technical term,” the Court should construe this term in accordance with BMS’s proposed construction. *Phillips*, 415 F.3d at 1315; *see also CCS Fitness*, 288 F.3d at 1366. Accordingly, given the clear intrinsic record, “a subject in need thereof” should be construed as “an animal, including a human, in need thereof.”

Apotex’s proposed construction of “any living organism” is much broader than how the term is defined in the ‘746 patent and is therefore improper. *See ERBE*, 566 F.3d at 1034 (“We generally do not construe claim language to be inconsistent with the clear language of the specification; ‘[u]sually, it is dispositive.’”) (citation omitted). In addition, Apotex once again seeks to inappropriately import the extraneous “two actors” limitation into the claims, arguing that this term requires diagnosis by “a second party.” Notably, Apotex fails to identify any

support for the addition of this “second party” limitation in the specification or the prosecution histories. Apotex’s proposed construction should therefore be rejected.

E. “of at least one compound of formula III or a salt thereof



This phrase appears in claim 7 of the ‘746 patent. Claim 7 is directed to a method for treating a protein tyrosine kinase-associated disorder with at least one compound of formula III or a salt thereof. The parties proposed constructions are set forth below:

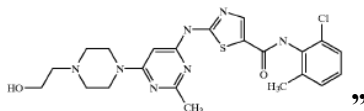
BRISTOL-MYERS CONSTRUCTION	APOTEX CONSTRUCTION
Plain meaning as understood by a person of ordinary skill in the art. “Salt” denotes acidic and/or basic salts formed with inorganic and/or organic acid and bases.	At least one compound falling within the scope of compounds that may result from formula III as further defined by the language of claim 7, or a salt thereof; where the term “salt” denotes acidic and/or basic salts formed with inorganic and/or organic acids and bases; including zwitterions (internal or inner salts) and quaternary ammonium salts; and further including both pharmaceutically-acceptable and other salts; prodrugs and solvates of the compound or salt thereof, and all stereoisomers of the compound or salt thereof. The claim term is also understood to include all polymorphs of the compound or salt thereof. The claim term is exclusive of those compositions containing one or more compounds not described by Formula III, including, but not limited to, for example, impurities.

BMS submits that this term should be construed in accordance with its ordinary and customary meaning as understood by one of skill in the art. The concept of claiming compounds with a formula is well accepted and requires no construction. *See, e.g., The Regents of Univ. Cal. v. Eli Lilly and Co.*, 119 F.3d 1559, 1568 (1997) (“In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus.”); *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 323 F.3d 956, 964 (Fed. Cir. 2002) (“showing that an invention is complete by disclosure of sufficiently detailed, relevant

identifying characteristics . . . *i.e.*, complete or partial structure. . .”). Accordingly, this claim term should be given its ordinary meaning. Further, as stated above, the ‘746 patent defines “salt” as denoting “acidic and/or basic salts formed with inorganic and/or organic acid and bases.” (Jorgensen Ex. A, col. 6, ll. 21-23.)

Apotex’s assertion that this term excludes impurities has absolutely no basis and directly contradicts the plain language of the claim. First, as discussed above, it is well recognized that all compounds, even after purification, will contain some amount of impurities. *See* Jorgensen ¶¶ 8-9. In addition, the language “at least one compound of Formula III” on its face allows for other ingredients. *See z4 Techs., Inc. v. Microsoft Corp.*, 507 F.3d 1340, 1349 (citing *Rhine v. Casio, Inc.*, 183 F.3d 1342, 1345 (Fed. Cir. 1999)) (“[u]se of the phrase ‘at least one’ means that there could be only one or more than one”). Apotex’s construction should therefore be rejected.

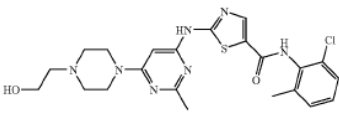
F. “The compound

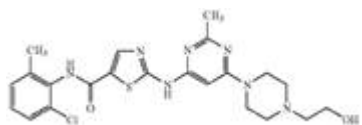


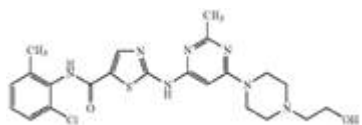
This phrase appears in claim 43 of the ‘746 patent and claim 1 of the ‘856 patent and is directed to the compound known as dasatinib. The parties’ proposed constructions are below:

BRISTOL-MYERS CONSTRUCTION	APOTEX CONSTRUCTION
<p>The compound represented by ‘N-(2-Chloro-6-methylphenyl)-2-[[6-[4-(2-hydroxyethyl)-1-piperazinyl]-2-methyl-4-pyrimidinyl]amino]-5-thiazolecarboxamide, and is the same as</p>	<p>A compound with the structure expressly identified in the claim, wherein this structure cannot represent a compound known as dasatinib.</p>

The chemical structure of claim 43 is represented by the chemical name ‘N-(2-Chloro-6-methylphenyl)-2-[[6-[4-(2-hydroxyethyl)-1-piperazinyl]-2-methyl-4-pyrimidinyl]amino]-5-

thiazolecarboxamide and is the same as , which as discussed above is



also equivalent to . *See* Jorgensen ¶¶ 10-12. In the specification, Example 455, the chemical name, ‘N-(2-Chloro-6-methylphenyl)-2-[[6-[4-(2-hydroxyethyl)-1-piperazinyl]-2-methyl-4-pyrimidinyl]amino]-5-thiazolecarboxamide, is specifically associated with the structure shown in claim 43. (Jorgensen Ex. A, Ex. No. 455, col. 213-14). This chemical name would inform one of ordinary skill of the chemical structure of the compound and all of the substituents at the various positions on the molecule, including the fact that there is a hydrogen bonded to the nitrogen of the amine and the nitrogen of the amide. *See* Jorgensen ¶¶ 11, 17, 19.

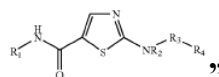
In addition, the U.S. Patent and Trademark Office (“PTO”) determined that claim 43 “claims the human drug product Sprycel[®] (dasatinib)” and was eligible for a patent term extension. *See* Request for Term Extension for U.S. Patent No. 6,596,746, dated Aug. 26, 2006 (BMS01358757-8771, at BMS01358760) (attached herein as Gannon Ex. D); Notice of Final Determination for U.S. Patent No. 6,596,746, dated April 21, 2011 (BMS01359426-28) (attached herein as Gannon Ex. E). Thus, Apotex’s argument that claim 43 cannot represent a compound known as dasatinib is baseless.

Apotex asserts that the claimed compound should be construed with the structure expressly identified in the claim and that it cannot represent dasatinib due to the omission of hydrogen atoms on the structure. However, as explained by Dr. Jorgensen, it is an acceptable convention in the field of chemistry to omit the hydrogen of amines and amides when drawing a chemical structure and a person of ordinary skill would understand that in the structure shown in claim 43, the nitrogen of the amine and the nitrogen of the amide are bonded to a hydrogen. *See* Jorgensen ¶¶

17-19. Indeed, the '746 patent illustrates hundreds of structures of chemical compounds without showing explicitly the hydrogen of amines or amides. *See* Jorgensen ¶¶ 17

Moreover, Apotex's construction is not supported by the proposed testimony of its expert Dr. Fernandez. He did not offer a construction of the claimed structure, but instead opines that the structure is indefinite. (Dkt. 51, Ex. E ¶¶ 2, 4). However, a claim is indefinite only if it is "insolubly ambiguous" and no "construction can properly be adopted." *Exxon*, 256 F.3d at 1375. This is clearly not the case here since a person of ordinary skill, as well as the PTO, understood the compound represented by the recited structure. *See* Jorgensen, ¶¶ 11, 17, 19.

G. "the compound of formula III or a salt thereof"

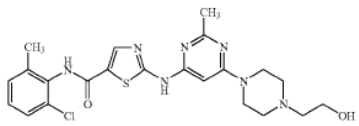


This phrase appears in claims 1 and 3 of the '875 patent, which are directed to methods to treat cancer with the compound of formula III. The parties' proposed constructions are below:

BRISTOL-MYERS CONSTRUCTION	APOTEX CONSTRUCTION
Plain meaning as understood by a person of ordinary skill in the art. "Salt" denotes acidic and/or basic salts formed with inorganic and/or organic acid and bases.	At least one compound falling within the scope of compounds that may result from formula III as further defined by the language of claim 1, or a salt thereof; where the term "salt" denotes acidic and/or basic salts formed with inorganic and/or organic acids and bases; including zwitterions (internal or inner salts) and quaternary ammonium salts; and further including both pharmaceutically-acceptable and other salts; prodrugs and solvates of the compound or salt thereof, and all stereoisomers of the compound or salt thereof. The claim term is also understood to include all polymorphs of the compound or salt thereof.

BMS submits that this term should be construed in accordance with its ordinary and customary meaning as understood by one of skill in the art. As discussed above, the concept of claiming compounds with a formula is well accepted and requires no construction. (*See supra* IV.E.) Further, the '875 patent defines "salt" as denoting "acidic and/or basic salts formed with inorganic and/or organic acid and bases." (Jorgensen Ex. C, col. 6, ll. 44-46.)

Apotex's construction is not understood and once again appears to be nothing but an attempt to anticipate arguments it would make regarding the infringement and validity of the patents in suit. Apotex's construction should therefore be rejected.



H. “a compound of formula IV [or salt thereof]”

This phrase appears in claims 2, 10 and 27 of the '875 patent.⁸ The parties' proposed constructions are set forth below:

BRISTOL-MYERS CONSTRUCTION	APOTEX CONSTRUCTION
Plain meaning as understood by a person of ordinary skill in the art.	The compound depicted by formula IV, generically known as dasatinib; or a salt thereof; wherein the term “salt” denotes acidic and/or basic salts formed with inorganic and/or organic acids and bases; including zwitterions (internal or inner salts) and quaternary ammonium salts; and further including both pharmaceutically-acceptable and other salts; prodrugs and solvates of the compound or salt thereof, and all stereoisomers of the compound or salt thereof. The claim term is also understood to include all polymorphs of the compound or salt thereof.

BMS submits that this term should be construed in accordance with its ordinary and customary meaning as understood by one of skill in the art. As discussed above, the concept of claiming compounds with a formula is well accepted and requires no construction. (*See supra* IV.E.) Further, as discussed, the '875 patent defines “salt” as denoting “acidic and/or basic salts formed with inorganic and/or organic acid and bases.” (Jorgensen Ex. C, col. 6, ll. 44-46.)

Once again, Apotex's construction is not understood and appears to be nothing but an attempt to anticipate arguments it would make regarding the infringement and validity of the patents in suit. Apotex's construction should therefore be rejected. In any event, Apotex does not dispute that this phrase recites the compound depicted by formula IV known as dasatinib. Accordingly, this claim term should be given its plain meaning.

⁸ Claims 2 and 10 do not include “or salt thereof”.

I. “wherein the cancer is resistant to treatment by STI-571” or “wherein the chronic myelogenous leukemia (CML) is resistant to STI-571”

This phrase appears in claims 9, 10, 12 and 27 of the ‘875 patent. These claims are directed to methods of treating cancer with compounds of formula III or formula IV wherein the cancer is resistant to treatment by STI-571. The parties’ proposed constructions are below:

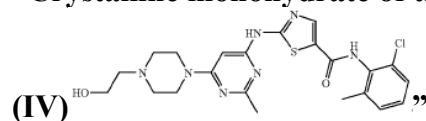
BRISTOL-MYERS CONSTRUCTION	APOTEX CONSTRUCTION
Wherein the cancer [or chronic myelogenous leukemia (CML)] exhibits resistance to treatment by STI-571	The claim term requires two actors: one, the subject in need of treatment; two, another person, likely a physician, nurse practitioner or other clinician, capable of determining if and who has determined that said cancer [or chronic myelogenous leukemia (CML)] in patient is resistant to treatment by STI-571; wherein STI- 571 is known as Gleevec™ (imatinib mesylate).

BMS’s proposed construction is supported by the specification and the accepted meaning of the term. The ‘875 patent discloses that the claimed compounds may be useful “in the treatment of cancers that are sensitive to and resistant to chemotherapeutic agents that target BCR-ABL and c-KIT, such as, for example, Gleevec® (STI-571).” (Jorgensen Ex. C, col. 28, ll. 26-38). The term “resistant” is defined in the dictionary as “giving or capable of resistance.” Merriam-Webster's Collegiate® Dictionary 1564 (Deluxe ed. 1998) (attached herein as Gannon Ex. F.) (BMS01380836-38). Accordingly, the Court should construe this claim consistent with the construction set forth by BMS -- “wherein the cancer [or chronic myelogenous leukemia (CML)] exhibits resistance to treatment by STI-571.”

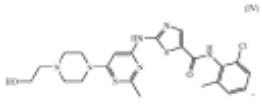
Apotex’s proposed construction again improperly seeks to add a limitation to the claims, stating that such claims should be construed to require “two actors.” (*See supra* IV.C.). Notably, Apotex fails to identify any support for its construction in the intrinsic record. Apotex’s construction should therefore be rejected.

IV. CONSTRUCTION OF TERMS IN THE '725 PATENT

A. “Crystalline monohydrate of the compound of formula



This phrase appears in claims 1, 3 and 12. These claims are directed to crystalline monohydrate compounds of formula IV. The parties proposed constructions are set forth below:

BRISTOL-MYERS CONSTRUCTION	APOTEX CONSTRUCTION
Plain meaning as understood by a person of ordinary skill in the art, <i>i.e.</i> , the monohydrate of the compound of formula IV in a crystalline form.	Raw material produced by process conditions presented in the specification, with a particular arrangement of the following compound:  in three dimensional space that has a certain degree of long range order, with a 1:1 molar arrangement of water to compound formally associated in a unit crystal cell lattice.

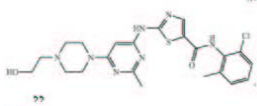
The above phrase is well-understood by those of ordinary skill in the art and requires no construction. To the extent that any construction is required, the Court should apply the plain and ordinary meaning as understood from the specification, namely, “the monohydrate of the compound of formula IV in a crystalline form.” Indeed, the specification discloses an example of the preparation of a crystalline monohydrate in Example 8. (Atwood Ex. A, col. 43, l. 30 - col. 45, l. 32.) *See* Declaration of Jerry Atwood in Support of Plaintiff’s Opening Claim Construction Brief (“Atwood”) ¶ 32. A monohydrate means a compound containing one molecule of water. *See* Atwood Ex. I (The American Heritage Dictionary for the English Language 1137 (4th ed. 2000) (defining “monohydrate” as “[a] compound, such as calcium chloride monohydrate, CaCl₂.H₂O, that contains one molecule of water.”)).

Apotex’s proposed construction has no support in the intrinsic record. There is nothing in the claim language itself, the specification or the prosecution history that limits the crystalline monohydrate of the compound of formula (IV) to “[r]aw material produced by process

conditions presented in the specification.” *See AFG Indus. v. Cardinal IG Co.*, 375 F.3d 1367, 1372-73 (Fed. Cir. 2004) (ruling it is improper to adopt a construction “that would impermissibly import a process limitation into a pure product claim”). Apotex’s construction should be rejected.

B. “which is characterized by an X-ray powder diffraction pattern substantially in accordance with that shown in FIG. 1”

This phrase appears in claim 1. The parties proposed constructions are set forth below:

BRISTOL-MYERS CONSTRUCTION	APOTEX CONSTRUCTION
Which is characterized by an x-ray powder diffraction pattern that is substantially identical to those shown in FIG. 1 taking into account variations due to measurement errors and dependent upon the measurement conditions employed, but not taking into account the exact order of intensity of the peaks. The ability to ascertain substantial identities of X-ray diffraction patterns is within the purview of one of ordinary skill in the art.	<p>The product being characterized must match the x-ray powder diffraction pattern presented in FIG. 1 of the patent specification, and further do so in such a way so as to uniquely identify the referenced “[c]rystalline monohydrate of the compound of formula (IV)</p> 

BMS’s proposed construction properly uses the specification to inform the meaning of the term. For example, the specification states that “[a]ny crystal forms that provide X-ray diffraction patterns substantially identical to those disclosed in the accompanying Figures fall within the scope of the present invention. The ability to ascertain substantial identities of X-ray diffraction patterns is within the purview of one of ordinary skill in the art.” (Atwood Ex. A, col. 42, ll. 8-13.) In addition, the patent specification discloses that

[o]ne of ordinary skill in the art will appreciate that an X-ray diffraction pattern may be obtained with a measurement error that is dependent upon the measurement conditions employed. In particular, it is generally known that intensities in a X-ray diffraction pattern may fluctuate depending upon the measurement conditions employed. It should be further understood that relative intensities may also vary depending upon experimental conditions and, accordingly, the exact order of intensity should not be taken into account. Additionally, a measurement error of diffraction angle for a conventional X-ray diffraction pattern is typically about 5% or less, and such degree of measurement error should be taken into account as pertaining to the aforementioned diffraction angles.

(Atwood Ex. A, col. 41, l. 58 - col. 42, l. 4.) BMS's construction takes into account variations in X-ray diffraction patterns that could occur from measurement errors and conditions. *Id. See* Atwood ¶¶ 34-35. And it takes into account the patent teaching that peak intensities may fluctuate and the exact order of intensity of the peaks should not be considered in comparing X-ray diffraction patterns. (Atwood Ex. A, col. 41, l. 58 - col. 42, l. 13) *See* Atwood ¶ 36.

BMS's proposed construction also takes into account the use of "substantially" which has been defined by the Federal Circuit as a descriptive term commonly used to avoid strict boundaries. *See, e.g., Playtex Products, Inc. v. Proctor & Gamble Co.*, 400 F.3d 901, 907 (Fed. Cir. 2005) (stating that the term "substantially" is a "descriptive term[] commonly used in patent claims to avoid a strict numerical boundary to the specified parameter."); *Cordis Corp. v. Medtronic AVE, Inc.*, 339 F.3d 1352, 1360 (Fed. Cir. 2003) (finding that the district court improperly imposed a numeric limit on the term "substantially uniform thickness" and construing it to mean "approximate uniform thickness."). Accordingly, the Court should construe this term in accordance with BMS's construction.

In contrast, Apotex's construction that "the product being characterized *must match* the x-ray powder diffraction pattern presented in FIG. 1 . . ." directly contradicts the claim language and the teachings in the specification. *See ERBE*, 566 F.3d at 1034 ("We generally do not construe claim language to be inconsistent with the clear language of the specification."). Apotex's construction of "must match" would also write out the words "substantially in accordance" from the claim. This is not proper. *See Bicon, Inc. v. Strauman Co.*, 441 F.3d 945, 951 (Fed. Cir. 2006) (rejecting a construction that would "read limitations . . . out of the claim," which would be "contrary to the principle that claim language should not [be] treated as meaningless"); *see also Warner-Jenkinson Co., Inc. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 29

(1997) (“Each element contained in a patent claim is deemed material to defining the scope of the patented invention....”). Apotex’s construction should therefore be rejected.

C. “The compound of claim 1” or “The compound of claim 3” or “A process for preparing the compound of claim 3” or “The compound of claim 9” or “The compound of claim 12”

This phrase appears in claims 2, 4, 5, 6, 7, 8, 9, 10, 11, 13, 14, 15 and 16. The parties proposed constructions are set forth below:

BRISTOL-MYERS CONSTRUCTION	APOTEX CONSTRUCTION
<p>Plain meaning as understood by a person of ordinary skill in the art, <i>i.e.</i>, the crystalline monohydrate of the compound of formula (IV). (Claims 2, 4, 5, 8-11, 13, 14, 15 and 16)</p> <p>Plain meaning as understood by a person of ordinary skill in the art, <i>i.e.</i>, a process for preparing the crystalline monohydrate of the compound of formula (IV). (Claims 6, 7)</p>	<p>The compound defined by claim 1, including all limitations of claim 1. (Claim 2)</p> <p>The compound that is identified and defined as such in claim 3; [which in turn is identified in claim 9]; this construction renders claim [4, 5, 8, 9, 10] invalid for improper dependency. (Claims 4, 5, 8-10, 13)</p> <p>To the extent the claim is construed as limited to a particular form, the claim is not enabled and/or not infringed because the crystal form no longer exists if it is to engage in any therapeutic activity. (Claims 4)</p> <p>A process that must occur in the United States for preparing. The term is vague and indefinite in the context of the claim. (Claims 6, 7)</p> <p>The compound that is identified and defined as such in claim 3; which in turn is identified in claim 9; this construction renders claim 10 invalid for improper dependency. (Claims 10, 11)</p> <p>The compound that is identified and defined as such in claim [9, 12]; this construction renders claim [14, 15, 16] invalid for improper dependency. (Claims 14-16)</p> <p>The compound that is identified and defined as such in claim [9, 12]; this construction renders claim [14, 15, 16] invalid for improper dependency. (Claims 14-16)</p>

The phrase “the compound of claim []” is well-understood by those of ordinary skill in the art. Thus, the Court should apply the plain and ordinary meaning of the phrase as understood by one of skill in the art based on the specification, namely, the monohydrate of the compound of formula IV in a crystalline form. Each time the phrase “the compound of claim []” or “the process for preparing the compound of claim []” is used in the ‘725 patent, it is referring to the monohydrate of the compound in a crystalline form. For example, claim 2, dependent from claim 1, recites a compound of claim 1 characterized by a differential scanning calorimetry

thermogram substantially in accordance with FIG. 2. (Atwood Ex. A, col. 48, ll. 64-67). The ‘725 patent states that FIG. 2 shows a DSC and TGA of “the monohydrate of the compound of Formula (IV).” (*Id.* at col. 45, ll. 15-16.) Indeed, the specification consistently makes it clear that “the compound of claim []” refers to the crystalline monohydrate of the compound of formula (IV). *See* Atwood, ¶¶ 47-51. Thus, reading the specification and claims in context dictates this term mean “the monohydrate of the compound of formula IV in a crystalline form.” *See Phillips*, 415 F.3d at 1314; *accord Pause Tech. LLC v. TiVo, Inc.*, 419 F.3d 1326, 1331 (Fed. Cir. 2005) (“proper claim construction . . . demands interpretation of the entire claim in context, not a single element in isolation.”) (citation omitted).

Apotex’s various proposed constructions are not constructions at all but arguments concerning the validity of the claims and sites where the process can be practiced. These constructions find no support in the claim language or the patent specification. Apotex’s proposed construction should therefore be rejected.

D. “which is characterized by differential scanning calorimetry thermogram and a thermogravimetric analysis substantially in accordance with that shown in FIG. 2”

This phrase appears in claim 2. The parties proposed constructions are set forth below:

BRISTOL-MYERS CONSTRUCTION	APOTEX CONSTRUCTION
Which is characterized by differential scanning calorimetry thermogram and thermogravimetric analysis patterns that are substantially identical to those shown in FIG. 2, having one peak at approximately 287° C and one broad peak between approximately 95° C and approximately 130° C. The ability to ascertain substantial identities of patterns is within the purview of one of ordinary skill in the art.	<p>The product being characterized must match both the differential scanning calorimetry thermogram and the thermogravimetric results presented in FIG. 2 of the patent specification, and further do so in such a way so as to uniquely identify the referenced “[c]rystalline monohydrate of the compound of formula (IV)</p> <div data-bbox="638 457 933 594" data-label="Chemical-Block"> </div> <p>At least the phrase “differential scanning calorimetry thermogram . . . in accordance with that shown in FIG. 2” is indefinite owing to the failure, in the patent specification to disclose the methodology for testing. (E.g., open pan, first run/second run).</p>

BMS’s proposed construction is based on the teachings of the specification as understood by a person of ordinary skill in the art. *See* Atwood ¶¶ 38-40. As disclosed in the ‘725 patent:

The monohydrate of the compound of formula (IV) is represented by the DSC as shown in FIG. 2. The DSC is characterized by a broad peak between approximately 95 C. and 130 C. This peak is broad and variable and corresponds to the loss of one water of hydration as seen in the TGA graph. The DSC also has a characteristic peak at approximately 287 C. which corresponds to the melt of the dehydrated form of the compound of formula (IV).

(Atwood Ex. A, col. 45, ll. 15-22). BMS’s proposed construction takes into account the “approximate” peak locations as described in the specification and as shown in FIG. 2. *Id.* In addition, a person of ordinary skill would take into account variations due to measurement errors and conditions when reading the DSC and TGA patterns; thus, the ability to ascertain substantial identities of such patterns is within the purview of one of ordinary skill. *See* Atwood ¶ 40.

In contrast, Apotex’s construction again contradicts the teachings of the specification and ignores words in the claim. Apotex proposes that “the product being characterized *must match* both the differential scanning calorimetry thermogram and the thermogravimetric results presented in FIG. 2.” This construction would write out the words “substantially in accordance”

from the claim, which, as stated above, is improper. *See Bicon*, 441 F.3d at 951. Further, Apotex's construction contradicts the specification which allows for consideration of variations due to measurement errors and conditions in comparing DSC and TGA patterns. *See Atwood* ¶¶ 40, 54, 59. Apotex's construction should be rejected.

E. “which is characterized by an x-ray powder diffraction pattern (Cu k_{α} γ =1.5418 Å at a temperature of about 23° C.) comprising four or more 2 θ values selected from the group consisting of: 18.0±0.2, 18.4±0.2, 19.2±0.2, 19.6±0.2, 21.2±0.2, 24.5±0.2, 25.9±0.2, and 28.0±0.2”

This phrase appears in claim 3. The parties proposed constructions are set forth below:

BRISTOL-MYERS CONSTRUCTION	APOTEX CONSTRUCTION
Which is characterized by XRPD pattern taken with Cu k_{α} λ =1.5418 Å at a temperature of about 23° C, having at least four 2 θ values selected from the group consisting of: 18.0±0.2, 18.4±0.2, 19.2±0.2, 19.6±0.2, 21.2±0.2, 24.5±0.2, 25.9±0.2, and 28.0±0.2.	<p>The product being characterized must uniquely identify the referenced “[c]rystalline monohydrate of the compound of formula (IV)</p> <div data-bbox="527 871 803 955" data-label="Chemical-Block"> </div> <p>And generate an x-ray powder diffraction pattern using the methodology provided (CuKα γ =1.5418 Å at a temperature of about 23° C.).</p> <p>The term “2θ values” is vague and indefinite.</p> <p>“selected from the group consisting of” is Markush language, but in the context of the claims is vague and indefinite;</p> <p>To the extent variance is permitted, it is not supported by the claims; is indefinite and not supported by the written description; and violates the Markush concept.</p>

BMS submits that the above phrase is well-understood by those of ordinary skill in the art, meaning “which is characterized by XRPD pattern taken with Cu k_{α} λ ⁹ =1.5418 Å at a temperature of about 23° C, having at least four 2 θ values selected from the group consisting of: 18.0±0.2, 18.4±0.2, 19.2±0.2, 19.6±0.2, 21.2±0.2, 24.5±0.2, 25.9±0.2, and 28.0±0.2.” (*See Atwood* ¶ 44.) In contrast, Apotex's proposed construction again seeks to import extraneous limitations into the claim and is not supported by the specification. Instead of offering a cogent

⁹ One having ordinary skill in the art would understand that “CuK α γ ” is “CuK α λ .” This is supported by the specification. (*See, e.g., Atwood Ex. A*, col. 25, ll. 14-21.) Further, a certificate correction was filed on May 11, 2010 correcting the typographical error. *See Atwood Ex. M*.

construction, Apotex's chooses to argue about the validity of the claims. Apotex's proposed construction should be rejected.

**F. “characterized by unit cell parameters approximately equal to the following:
Cell dimensions: $a(\text{\AA})=13.8632(7)$; $b(\text{\AA})=9.3307(3)$; $c(\text{\AA})=38.390(2)$;
Volume= $4965.9(4) \text{\AA}^3$
Space group Pbca
Molecules/unit cell 8
Density (calculated) (g/cm^3) 1.354”**

This phrase appears in claim 5. The parties proposed constructions are set forth below:

BRISTOL-MYERS CONSTRUCTION	APOTEX CONSTRUCTION
Plain meaning as understood by a person of ordinary skill in the art.	This term is indefinite, as it is internally contradictory to and with the underlying independent claim and the other claim text, and “approximately equal to” is likewise vague and indefinite.

BMS submits that the above phrase is well-understood by those of ordinary skill in the art and requires no construction. As explained by Dr. Atwood, characterizing crystalline compounds by unit cell parameters is well understood by one of ordinary skill. *See Atwood ¶ 46.*

Rather than proposing a construction for this claim term, Apotex baldly asserts that it is indefinite, but fails to articulate a proper basis for this contention. Apotex's objection to the term “approximately equal to” is baseless. Use of terms such as “approximately” to avoid strict boundaries is permitted and commonly used in patents. *See Quantum Corp. v. Rodime, PLC*, 65 F.3d 1577, 1581 (Fed. Cir. 1995) (“The addition of ‘approximately’ which means ‘reasonably close to,’ eliminates the precise lower limit of [a] range, and, in so doing extends the scope of the range.”); *Merck & Co. v. Teva Pharmaceuticals USA, Inc.*, 395 F.3d 1364, 1372 (Fed. Cir. 2005) (construing “approximately” to mean “about.”)

G. “wherein the compound is substantially pure”

This phrase appears in claims 8, 15 and 16. The parties proposed constructions are below:

BRISTOL-MYERS CONSTRUCTION	APOTEX CONSTRUCTION
The compound itself having a purity greater than 90 percent. The “substantially pure” compound may be employed in pharmaceutical compositions to which other desired components are added, for example, excipients, carriers, or active chemical entities of different molecular structure.	<p>The term is indefinite, particularly in the context of the claim language. Apotex recognizes that the specification states, “The present invention describes crystalline forms of the compound of formula (IV) in substantially pure form. As used herein, ‘substantially pure’ means a compound having a purity greater than 90 percent, including 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, and 100 percent.”</p> <p>However, a compound in and of itself cannot be “90 percent” or “99 percent” pure. A compound is what it is.</p> <p>A bulk drug substance, for example, may be a composition that contains 99% by measured weight of a particular compound; a different composition would be one that contains 99% molar amounts of a particular compound; a different composition would be one that contains 99% of a particular compound by volume. All would produce different results in the context of an infringement analysis.</p> <p>Further, a monohydrate crystal by definition cannot be at least 99% pure compound, because such material will necessarily contain water on a 1:1 molar ratio basis.</p>

BMS’s proposed construction is expressly supported by the specification. The ‘725 patent defines “substantially pure” as “meaning a compound having purity greater than 90 percent. . . .” (Atwood Ex. A, col. 15, ll. 28-40). The specification further provides an example of a crystalline form of the compound of formula (IV) as being “substantially pure in having a purity greater than 90 percent, where the remaining less than 10 percent of material comprises other form(s) of the compound of the formula (IV), and/or reaction and/or processing impurities arising from its preparation.” *Id.* In addition, the specification teaches that a crystalline form of the compound of the formula (IV) in substantially pure form may be “employed in pharmaceutical compositions to which other desired components are added, for example, excipients, carriers, or active chemical entities of different molecular structure.” *Id.* Thus, the Court should construe this term in accordance with BMS’s proposed construction.

While recognizing that the specification provides an explicit definition for this claim term, Apotex declines to offer a construction and instead argues that this term is indefinite. Apotex asserts that “a compound in and of itself cannot be ‘90 percent’ or ‘99 percent’ pure. A

compound is what it is.” This argument is unfounded and ignores the plain teaching of the specification. Further, as explained by Dr. Jorgensen, there is no such thing as a 100% pure compound. *See* Jorgensen ¶¶ 8-9. Use of terms such as “pure” or “substantially pure” to describe compounds is common and permitted under the law. *See In re Kratz*, 592 F.2d 1169, 1173-74 (C.C.P.A. 1979); *see also Evans Medical Ltd. v. American Cyanamid Co.*, 215 F.3d 1347, 1999 WL 594310, at * 5-6 (Fed. Cir. 1999) (unpublished) (construing “purified” to mean “in an amount greater than fifty percent”). Apotex’s indefiniteness argument should be rejected. *See Ortho-McNeil*, 348 F. Supp. 2d at 729-30 (rejecting the contention that a patent claiming a chemical compound must specify an exact level of purity to avoid a finding of indefiniteness).

H. “being further characterized by a differential scanning calorimetry having a broad peak between approximately 95° C and 130° C”

This phrase appears in claims 9¹⁰ and 12. The parties proposed constructions are below:

BRISTOL-MYERS CONSTRUCTION	APOTEX CONSTRUCTION
Characterized by a differential scanning calorimetry having a broad peak between about 95° C and about 130° C. This peak can be variable but corresponds to the loss of one water of hydration on thermogravimetric analysis.	The product being characterized must match the stated results. The term “broad peak” is vague and indefinite. The term “peak” is not routinely used in the context of analyzing differential scanning calorimetry data. To the extent the term is intended to refer to endotherms or exotherms that can appear in a DSC trace, the claim language is indefinite and/or non-enabled. “Approximately” is indefinite in the context of the claims. At least the phrase “differential scanning calorimetry” is indefinite owing to the failure to disclose the methodology for testing. (E.g., open pan, first run/second run).

BMS’s proposed construction is fully supported by the specification:

The monohydrate of the compound of formula (IV) is represented by the DSC shown in FIG 2. The DSC is characterized by a broad peak between approximately 95 °C. and 130 °C. This peak is broad and variable and corresponds to the loss of one water of hydration as seen in the TGA graph.

¹⁰ In claim 9, 130 °C was erroneously printed as 13 °C. A person of ordinary skill would understand that this is a typographical error. A certificate of correction filed on May 11, 2010 corrected this error. *See* Atwood Ex. M.

(Atwood Ex. A, col. 45 ll. 15-19). *See* Atwood ¶¶ 38, 39, 53, 54.

Apotex's argument that "[t]he product being characterized must match the stated results" would write out the word "approximately" in the claim and ignores the teaching in the specification that the broad peak is between *approximately* 95 °C. and 130 °C. The term "approximately" cannot be construed to mean "must match." *See Quantum Corp.*, 65 F.3d at 1581; *Merck.*, 395 F.3d at 1372; *UCB, Inc., v. KV Pharm. Co.*, 2009 WL 2524519, *6 (D. Del. 2009) (refusing to construe "approximately" as narrowly as "almost exactly"). Apotex's construction should therefore be rejected.

Apotex's objections to the terms "broad peak," "approximately," and "differential scanning calorimetry" are unfounded and appear to be an attempt to avoid addressing claim construction. As explained by Dr. Atwood, these terms are definite and would have been understood by a person of ordinary skill in the art. *See* Atwood ¶¶ 41, 42, 54.

I. "which corresponds to the loss of one water of hydration on thermogravimetric analysis"

This phrase appears in claims 9 and 12. The parties' proposed constructions are below:

BRISTOL-MYERS CONSTRUCTION	APOTEX CONSTRUCTION
Which corresponds to a weight loss attributable to one water of hydration on thermogravimetric analysis	<p>The claim language makes no sense in context, because a "compound" does not lose water.</p> <p>In general, if the claim were not internally contradictory, the language out of context would indicate that there is a peak in the DSC that must correspond and otherwise perfectly align to a TGA test result on the same sample being tested in which a precise, specific ratio of molecule(s) of water that constituted water formally associated in the unit cell of a crystal lattice is released (e.g., lost) in the specified test period.</p> <p>This claim language is vague and indefinite in the context of the remainder of the claim.</p>

As explained by Dr. Atwood, one of ordinary skill would understand this term to mean that the broad peak between approximately 95°C and 130°C corresponds to a weight loss attributable to one water of hydration on thermogravimetric analysis. This construction is fully

supported by the specification. (Atwood Ex. A, col. 45, ll. 16-19.) *See* Atwood ¶¶ 56-57. Rather than proposing a construction for this claim term, Apotex contends this term is indefinite. As explained by Dr. Atwood, this contention has no merit. *See* Atwood ¶ 57.

J. “which is further characterized by a weight loss of 3.48% by thermogravimetric analysis between 50° C and 175° C”

This phrase appears in claim 10. The parties’ proposed constructions are set forth below:

BRISTOL-MYERS CONSTRUCTION	APOTEX CONSTRUCTION
Which is further characterized by a weight loss of 3.48% by thermogravimetric analysis between 50° C and 175° C, taking into account variations due to measurement errors and dependent upon the measurement conditions employed.	In isolation, the phrase would refer to material that is being subjected to the testing. In general, if the claim were not internally contradictory, the language out of context would indicate that there is an instrumental measured weight loss of the stated amount being sampled between the stated temperature range. However, this claim language is vague and indefinite in the context of the remainder of the claim. The “weight loss” claim language makes no sense in context, or is not enabled, because a “compound” does not lose weight.

BMS’s proposed construction properly uses the specification to inform the meaning of the term. The ‘725 patent specification explicitly states:

The TGA shows a 3.48% weight loss from 50 C. to 175 C. The weight loss corresponds to a loss of one water of hydration from the compound of Formula (IV).

(Atwood Ex. A, col. 45, ll. 25-28). One of ordinary skill would understand this term to mean being further characterized by a weight loss of 3.48% by thermogravimetric analysis between 50° C and 175° C, taking into account variations due to measurement errors dependent upon the measurement conditions employed. *See* Atwood ¶ 59.

Again, rather than proposing a construction for this term, Apotex contends it is indefinite, but has not articulated any cogent basis for this contention. Apotex blithely states “a ‘compound’ does not lose weight.” (Gannon Ex. B, at 46.) However, as explained by Dr. Atwood, one having ordinary skill would understand that the weight loss corresponds to the loss

of water from the monohydrate. *See* Atwood ¶ 56. BMS submits that this claim element is not indefinite and is fully understandable as defined by the specification.

K. “wherein the differential scanning calorimetry further has a peak at approximately 287° C”

This phrase appears in claim 11. The parties’ proposed constructions are set forth below:

BRISTOL-MYERS CONSTRUCTION	APOTEX CONSTRUCTION
Characterized by differential scanning calorimetry with a peak located at about 287° C which corresponds to the melt of the dehydrated form of the compound of formula (IV)	<p>The product being characterized must match the stated results.</p> <p>The term “broad peak” is vague and indefinite. The term “peak” is not routinely used in the context of analyzing differential scanning calorimetry data. To the extent the term is intended to refer to endotherms or exotherms that can appear in a DSC trace, the claim language is indefinite and/or non-enabled.</p> <p>“Approximately” is indefinite in the context of the claims.</p> <p>At least the phrase “differential scanning calorimetry” is indefinite owing to the failure to disclose the methodology for testing. (E.g., open pan, first run/second run).</p>

BMS’s proposed construction is fully supported by the specification:

The DSC also has a characteristic peak at approximately 287°C. which corresponds to the melt of the dehydrated form of the compound of formula (IV).

(Atwood Ex. A, col. 45, ll. 21-23). *See* Atwood ¶ 61. Thus, the Court should construe this term in accordance with BMS’s proposed construction.

Apotex contends that “the product being characterized *must match* the stated results.” (Emphasis added). Once again, Apotex seeks to write out words from the claim and ignores the specification. Under Apotex’s construction, the term “about” in the claim would be rendered meaningless. Further, rather than offering a cogent construction, Apotex again contends that various terms are indefinite. As explained by Dr. Atwood, Apotex’s contentions are baseless.

V. CONCLUSION

For the reasons discussed above, BMS respectfully requests that the Court adopt its proposed constructions.

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Respectfully submitted,

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